

REMARKS

Formal Matters

With entry of this amendment, claims 18, 19, and 23-60 are pending in the above-identified application. Claims 26, 28, 34-45, and 47-51 have been withdrawn from consideration. Claims 21 and 22 are canceled without prejudice to Applicant's right to prosecute the subject matter of the canceled claims in a related co-pending application. In addition, claim 18 is amended to recite "... a construct which is formulated as a pill, a capsule, or a tablet ..." to further expedite prosecution of the instant application. Support for this amendment is found in the specification at, for example, page 33, lines 10 and 11. No new matter is added by this amendment.

Interview Summary

Applicants thank the Examiner for the teleconferences of August 20, 2003 with the undersigned, during which the submission of proofs relating to enablement issues as well as certain amendments to place the claims in better form for allowance were discussed. The present amendment serves to enter the amendments discussed. Further, attached hereto are copies of the Declarations Under 37 C.F.R. § 1.132 of Stephen S. Rothman (Exhibit 1) and Leslie Benet (Exhibit 2), which were previously submitted in the related application USSN 09/254,988. Submission of these declarations serves to provide the requisite proofs discussed relating to issues under 35 U.S.C. § 112, first paragraph.

Claim Rejections under 35 USC §112, First Paragraph

Claims 18, 19, 23-25, 27, 29-33, 46, and 52-60 stand rejected under 35 U.S.C. § 112, first paragraph, the Examiner believing that the specification does not provide enablement for the claimed invention.

As discussed in the Interview of August 20, 2003, similar issues were resolved in the prosecution of the parent application (USSN 09/254,988), which issued at U.S. Patent No. 6,258,789. The application as filed already shows that therapeutic results can be achieved using the claimed methods. Further, as discussed in the Interview, Declarations Under 37 C.F.R. § 132 of Stephen S. Rothman and Leslie Benet were submitted showing that oral delivery is enabled by the specification as filed.

Therefore, in accordance with the Interview of August 20, 2003, and further with the submission of the Rothman and Benet Declarations, attached hereto as Exhibits 1 and 2, Applicants respectfully submit that the pending claims are enabled by the specification as required under 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request that the Examiner withdraw the rejection of claims 18, 19, 23-25, 27, 29-33, 46, and 52-60 as lacking enablement under 35 U.S.C. § 112, first paragraph.

Claim Rejections under 35 USC §102

Claims 18, 19, 23-25, 27, 29-33, 46, and 52-60 stand rejected under 35 U.S.C. 102 (e) as being anticipated by Mathiowitz *et al.*

Initially, Applicants note that provisional application USSN 60/001,365, which was filed July 21, 1995 and to which Mathiowitz *et al.* claim priority, contains no disclosure of any methods for gene delivery, nor does it discuss nucleic acid constructs or their encapsulation in microparticles. Therefore, with respect to any claims directed to a method of gene delivery, the effective date of Mathiowitz *et al.* under 35 U.S.C. § 102(e) is the actual filing date of the non-provisional application from which the patent issued, *i.e.*, July 3, 1996.

Accordingly, while Applicants disagree with the Examiner's stated reasons for the instant rejection, Applicants have attached herewith a Declaration Under 37 C.F.R. § 1.131 by

Drs. Michael German, Stephen Rothman, and Ira Goldfine ("German *et al.* Declaration") (Exhibit 3), which shows a date of invention for the instant claimed subject matter prior to the July 3, 1996 filing date of Mathiowitz *et al.* The attached German *et al.* Declaration and supporting Declaration of Andrea Eubanks Under 37 C.F.R. § 1.132 (Exhibit I) are unsigned. Fully executed copies of these declarations will be provided once they are received.

The German *et al.* Declaration shows that Applicants' invention was conceived by Drs. German, Rothman, and Goldfine prior to July 3, 1996. (See Exhibit 3, ¶¶4-6; Exhibits A-C.) Following their conception, Drs. German, Rothman, and Goldfine carried out diligent efforts to reduce the invention to practice. These diligent efforts commenced on a date no later than before July 3, 1996, and continued until the filing of U.S. Patent Application No. 08/717,084 (herein "the '084 Application," the priority document for the '323 Application) on September 20, 1996. (Exhibit 3, ¶¶8-15. See Exhibits D-I.) The claimed invention was at least constructively reduced to practice by the filing of the '084 Application on September 20, 1996.

Applicants' work toward reduction to practice included studies of the delivery of human growth hormone (hGH) to the bloodstream by injecting a vector encoding hGH into the intestinal lumen. (Exhibit 3, ¶9.) These experiments were conducted before July 3, 1996. Results from at least one of these studies are described more fully in the '323 Application (see Examples 1 and 2). (*Id.*)

Also prior to July 3, 1996, Filemon Sorillo Dela Cruz ("Mr. Cruz"), a summer student in Dr. German's lab during the summer of 1996, began the construction of a Green Fluorescence Protein ("GFP") vector for additional *in vivo* studies. (*Id.*, ¶10. See Exhibit D.) The goal was to use the GFP vector to confirm, as well as to precisely track, intestinal cell expression of a construct delivered to the intestinal lumen. Mr. Cruz performed work on construction of the GFP vector commencing no later than July 1, 1996, and continuing at least until August 25, 1996, when Mr. Cruz returned to school for the Fall Semester at Reed College in Oregon. (Exhibit 3, ¶10. See Exhibit D).

In addition to studies in the lab, Applicants worked with Carol Francis, a patent agent with Fish and Richardson P.C., to diligently prepare the '084 Application

commencing no later than July, 1996, and continuing until September 20, 1996. (Exhibit 3, ¶11. *See Exhibits E-I.*) A draft of the '084 Application was reviewed at least by Dr. Rothman before July 29, 1996, when Dr. Rothman communicated his comments regarding the draft to Carol Francis. (*See Exhibit 3, ¶12; Exhibit E.*) These comments were incorporated into the draft by August 8, 1996, when Carol Francis forwarded the revised draft to the inventors for further review and comments. (*See Exhibit 3, ¶12; Exhibits E, G, and H.*) By August 13, 1996, Dr. Rothman had reviewed the revised draft and forwarded his comments to Carol Francis. (*See Exhibit 3, ¶13; Exhibits F & H.*) By August 20, 1996, Carol Francis had further revised the draft to incorporate Rothman's comments as well as additional data earlier provided by Dr. Rothman. (*See Exhibit 3, ¶¶13 & 14; Exhibit H.*) As of August 27, 1996, Carol Francis had further reviewed and forwarded the new draft to the inventors. Also as of August 27, 1996, Carol Francis was working on the Information Disclosure Statement (IDS) to file with the '084 Application. (*See Exhibit 3, ¶14; Exhibit H.*) Subsequent to receiving the new draft, Applicants continued to correspond with Carol Francis regarding the Application. The final version of the '084 Application was filed September 20, 1996.

In light of the above, Applicants respectfully submit that Mathiowitz *et al.* is not prior art with respect to the instant claims. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 18, 19, 23-25, 27, 29-33, 46, and 52-60 under 35 U.S.C. § 102(e).

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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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By:   
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